CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-111

MICROBIOLOGY REVIEW

DIVISION OF CHEMISTRY I
OFFICE OF GENERIC DRUGS

Microbiologist's Review #3

October 27, 1998

A. 1. ANDA: **75-111**

APPLICANT: Alpharma
U.S. Pharmaceuticals Division
Attention: Vincent Andolina
The Johns Hopkins Bayview Campus
333 Cassell Drive, Suite 3500
Baltimore, Maryland 21224

MANUFACTURER:

2. PRODUCT NAMES: **Ipratropium Bromide Inhalation Solution**

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:

Sterile **0.02%** aqueous solution for nebulization

4. METHOD(S) OF STERILIZATION:

5. PRINCIPLE INDICATIONS: Maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease, including chronic bronchitis and emphysema

6. PHARMACOLOGICAL CATEGORY: Bronchial dilator

B. 1. DATE OF INITIAL SUBMISSION:

April 11, 1997 (Received by OGD on 4/13/97)

2. DATE OF AMENDMENT: **October 16, 1998**
Subject of this Review **(Received by OGD on 10/19/98)**

3. RELATED DOCUMENTS: None

4. ASSIGNED FOR REVIEW: 9/27/98

C. REMARKS: The subject amendment is the response to the microbiology deficiencies presented in the FAX Amendment dated October 9, 1998.

D. CONCLUSIONS: The submission is recommended for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes".

10/27/9

Andrea S. High, Ph.D.

cc:

[illegible] M. Fanning, K. Patel, F. Fang/F. Holcombe, Jr.

Revised
10/29/98

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releasable.

Micro Rev. 3

10/27/98

DIVISION OF CHEMISTRY I
OFFICE OF GENERIC DRUGS

Microbiologist's Review #2

September 14, 1998

A. 1. ANDA: **75-111**

APPLICANT: Alpharma
U.S. Pharmaceuticals Division
Attention: Vincent Andolina
The Johns Hopkins Bayview Campus
333 Cassell Drive, Suite 3500
Baltimore, Maryland 21224

MANUFACTURER:

2. PRODUCT NAMES: **Ipratropium Bromide Inhalation Solution**

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:

Sterile **0.02%** aqueous solution for nebulization

4. METHOD(S) OF STERILIZATION:

5. PRINCIPLE INDICATIONS: Maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease, including chronic bronchitis and emphysema

6. PHARMACOLOGICAL CATEGORY: Bronchial dilator

B. 1. DATE OF INITIAL SUBMISSION:

April 11, 1997 (Received by OGD on 4/13/97)

2. DATE OF AMENDMENT: **February 19, 1998**
Subject of this Review **(Received by OGD on 2/20/98)**

3. RELATED DOCUMENTS: None

4. ASSIGNED FOR REVIEW: 9/10/98

C. REMARKS: The subject amendment is the response to the microbiology deficiencies presented in the correspondence dated September 22, 1997.

D. CONCLUSIONS: The submission is not recommended for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes" and "Microbiologist's Comments to be Provided to the Applicant."

9/15/98
Andrea S. High, Ph.D.

cc: ANDA

be, Jr.

9/15/98

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Micro Rev. 2
9/14/98

DIVISION OF CHEMISTRY I
OFFICE OF GENERIC DRUGS

Microbiologist's Review #1

June 5, 1997

A. 1. ANDA: **75-111**

APPLICANT: Alpharma
U.S. Pharmaceuticals Division
Attention: Vincent Andolina
The Johns Hopkins Bayview Campus
333 Cassell Drive, Suite 3500
Baltimore, Maryland 21224

MANUFACTURER:

2. PRODUCT NAMES: **Ipratropium Bromide Inhalation Solution**

3. DOSAGE FORM AND ROUTE OF ADMINISTRATION:

Sterile **0.02%** aqueous solution for nebulization

4. METHOD(S) OF STERILIZATION:

5. PRINCIPLE INDICATIONS: Maintenance treatment of bronchospasm associated with chronic obstructive pulmonary disease, including chronic bronchitis and emphysema

6. PHARMACOLOGICAL CATEGORY: Bronchial dilator

B. 1. DATE OF INITIAL SUBMISSION:

April 11, 1997 (Received by OGD on 4/13/97)
- Subject of this Review

2. DATE OF AMENDMENT: N/A; no amendments containing sterility assurance information were submitted by the time of this review

3. RELATED DOCUMENTS:

4. ASSIGNED FOR REVIEW: June 4, 1997

C. REMARKS: The information provided in the application was insufficient to determine if the applicant is taking the necessary steps to ensure the sterility of the subject drug product (Ipratropium Bromide Inhalation Solution 0.02%). For example, validation data were not provided for the steam-in-place process used to sterilize the . . achine, batch tanks and transfer lines.

D. CONCLUSIONS: The submissions are therefore not recommended for approval on the basis of sterility assurance. Specific comments are provided in "E. Review Notes" and "Microbiologist's Comments to be Provided to the Applicant."

Kenneth H. Muhvich 6/5/97.
Kenneth H. Muhvich, Ph.D.

ated
6/10/97

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Micro Review

6/5/97